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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/821,139	03/29/2001	Laura S. Lehman	7960-131	5628

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PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER
HAGHIGHATIAN, MINA

ART UNIT	PAPER NUMBER
1616	3

DATE MAILED: 02/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/821,139	LEHMAN ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03/29/01* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-11 and 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the limitation "said daily dosage" of claim 1. There is insufficient antecedent basis for this limitation in the claim. Claim 1 does not recite a "daily dosage". Claims 7, 10, 17 and 18 are rejected for analogous reasons. Claims 8, 9, 11,19 and 20 are rejected for depending on a rejected claim. Claim 17 is vague and indefinite because it contains range in a range. The ranges in the parentheses are further limitations of the ranges preceding them. Claim 18 is vague due to the typing error "about 1 weeks to about 8 weeks".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-12 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marketing Authorization for Pramidin (hereinafter Pramidin).

Pramidin discloses Pramidin 10 and Pramidin 20 compositions, where each ml solution contains metoclopramide hydrochloride monohydrate, corresponding to 200 or 400 mg metoclopramide free base respectively. Pramidin also contains purified water and other ingredients such as sorbitol and sodium acetate, thus meeting limitations of instant claims 1 and 12.

Pramidin is supplied in nasal spray form, and is indicated for therapeutic uses such as in nausea and vomiting induced by antineoplastics and other medications, digestive disorders and symptomatologic treatment of gastro-esophageal reflux, of duodenal-gastric biliary reflux and gastroparesis of various origin such as diabetic neuropathy, etc, thus meeting instant claims 1 and 15-17.

Dosage of Pramidin recommended for treatment of functional dyspepsia or other disorders of gastrointestinal motility is 1 puff of 10 mg in the same nostril 2-3 times daily (20-30mg). The drug must be administered before meals. For treatment of nausea/vomiting dosage is recommended at 20 mg in each nostril 3 times a day

(120mg). In cases of delayed nausea/vomiting the dosage is 120-160mg/day, thus meeting instant claims 2-11.

The instruction for use are also described.

Although the Pramidin document is more directed to the preparation than the method of treatment, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to have implemented slight modifications to the teachings in order to have obtained a method of treatment for a known product and disorder.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robins (product information on Reglan®) in view of Wenig (4,624,965).

Robins discloses metoclopramide monohydrochloride monohydrate in tablet, syrup and solution for injection. Metoclopramide is said to stimulate motility of the upper gastrointestinal tract without stimulating gastric, biliary or pancreatic secretions (see bottom of page 2). Robins also discloses that Reglan® (metoclopramide hydrochloride) is indicated for the relief of symptoms associated with acute and recurrent diabetic gastric stasis. The usual manifestations of delayed gastric emptying (e.g, nausea, vomiting, heartburn, persistent fullness after meals and anorexia) appear to respond to Reglan® within different time intervals, thus meeting limitations of instant claims 15-17 (see Indications and Usage on page 5).

Robins also discloses the appropriate dosages for the use of metoclopramide.

For the relief of symptoms associated with diabetic gastroparesis, 10mg of metoclopramide 30 minutes before each meal and at bedtime for two to eight weeks. Lower doses (2.5- 5 mg) or 0.1 mg/kg are recommended for pediatric patients and elderly, thus meeting limitations of claims 2-4, 6-8, 10-12 and 18-20 (see page 12).

Robins also discloses that metoclopramide solutions can be mixed with other active agents(drugs) such as cimetidine, mannitol, ascorbic acid, clindamycin, insulin etc, thus meeting instant claim 14 (see page 13). Robins lacks teachings on nasal preparations of metoclopramide.

Wenig teaches nasal administration of known anti-nausea and anti-emetic therapeutic agents and dosage forms useful for such administration. Metoclopramide is one of the preferred compounds for use in the nasal preparation because when low dosages are administered nasally high blood levels are rapidly achieved and maintained for a long period of time. Preferred nasal dosage forms are solutions, suspensions and gels, which normally contain a major amount of water (preferably purified water) in addition to the active agent, thus meeting claim 12. If desired, sustained release nasal compositions, e.g, sustained release gels, or when a more highly insoluble form is desired, a long chain carboxylic acid salt of the desired drugs can be conveniently employed, thus meeting claim 13 (col. 5, lines 8-12; 44-60).

Wenig discloses compositions for nasal drops or nasal spray. Composition C is shown to contain metoclopramide, water and additives which bring the final concentration to 10 mg/ 0.2 ml (see Example 1 in column 6).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the Reglan® preparations of Robins by using the nasal administration of metoclopramide taught by Wenig with the reasonable expectations of preparing a nasal preparation of metoclopramide for treating gastroparesis, which is pain free, economical and more efficient than oral administration.

Claims 1-20 rejected under 35 U.S.C. 103(a) as being unpatentable over Robins and in view of Psilogenis (5,760,086).

Robins, discussed above, lacks teachings on nasal preparations of metoclopramide.

Psilogenis teaches a method for the prophylactic management of delayed emesis by the use of metoclopramide nasal spray. Psilogenis teaches compositions, dosages, duration of therapy and method of administration of the said nasal spray (see whole document).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have combined the teachings of Robins and the composition and method of treatment of Psilogenis to prepare a nasal spray containing meoclopramide for the treatment of gastroparesis because of the disclosed benefits.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure, Tyers (5,578,632).

Tyers discloses the use of anti-emetic agents such as metoclopramide for stimulation of gastric motility. Tyres also discloses a method of treatment for the relief of nausea and vomiting, and/or the promotion of gastric emptying e.g. for the relief of gastrointestinal disorders associated with gastric stasis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 703-308-6330. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

Mina Haghighatian
February 4, 2002

JOSE' G. DEES
SUPERVISORY PATENT EXAMINER
1616